Faculty of Computer Science and Information Technology

Mathematical Model Incorporating Individuals' Trust, Vaccination Decision and Wane of Immunity for Establishing Herd Immunity

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DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.

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ABSTRACT

Infectious diseases are the main public health concerns worldwide. In controlling the re-emergence of infectious diseases, public health relies on achieving the herd immunity establishment in the population. The herd immunity is formed by having enough number of immune individuals in the population to reduce the transmission of infectious diseases and indirectly protect susceptible individuals against infection. There are two factors that affect herd immunity namely individuals' trust in public health and vaccines as well as wane of immunity in individuals. As these factors are modelled separately in most infectious disease models, this research aims to consolidate both individuals' trust in public health and vaccines as well as wane of immunity in individuals into one epidemiological model in maintaining herd immunity. The model in the research is known as Susceptible-Infected-Recovered-Trust-Vaccinated-Waned (SIRTVW) model. The SIRTVW model formulation into Equation-Based Model (EBM) with non-linear Ordinary Differential Equation (ODE) and Individual-Based Model (IBM) with rules assigned to the individuals have been implemented by using MATLAB (function ODE solver: ode15s) and NetLogo respectively. In addition, the integration of imitation dynamics based on game theory into EBM and IBM assists the vaccination decision of individuals. The verification and validation of EBM and IBM apply parameter sensitivity analysis and performance indicators such as accuracy percentage measurement metric of Root Mean Square Percentage Error (RMSPE) and execution time. Based on EBM and IBM simulations by using the actual parameter of Pertussis infectious disease in Malaysia, around 70% of individuals in EBM and 80% of individuals in IBM must acquire trust towards public health and vaccines to generate the optimum simulation results when validated to the actual prevalence. The RMSPE of 22.31% in IBM is lower than RMSPE of 56.12% in EBM due to the heterogeneity of individuals in

IBM of which EBM does not consider. As IBM mimics the actual prevalence, the 36.36% slower IBM simulation than EBM is acceptable. Furthermore, the individuals' trust towards public health and vaccines as well as the individuals' tendency to protect themselves against infection can reduce the transmission of infectious diseases in the population. In relation with herd immunity, a modified herd immunity threshold formula has been derived from SIRTVW model. The modification on the herd immunity threshold formula results in different threshold values due to sensitivity of certain parameters included in the formula. As herd immunity threshold is used to determine the minimum number of individuals that should be immune to induce herd immunity, the herd immunity threshold from the modified formula provides new insights for the establishment of herd immunity. It is very important to maintain the herd immunity establishment in the population as the disappearance of herd immunity becomes a barrier in controlling the transmission of infectious diseases.

Keywords: Herd immunity, herd immunity threshold, individuals' trust, wane of immunity, infectious disease modelling

Model Matematik Menggabungkan Keyakinan Individu, Keputusan Vaksinasi dan Pengurangan Imuniti untuk Menubuhkan Imuniti Kelompok

ABSTRAK

Penyakit berjangkit menjadi kebimbangan kesihatan awam di seluruh dunia. Dalam pengawalan kemunculan semula penyakit berjangkit, kesihatan awam bergantung kepada pencapaian penubuhan imuniti kelompok dalam populasi. Imuniti kelompok dibentuk dengan mempunyai bilangan individu imun yang cukup dalam populasi untuk mengurangkan penularan penyakit berjangkit dan secara tidak langsung melindungi individidu yang terdedah terhadap jangkitan. Terdapat dua faktor yang mempengaruhi imuniti kelompok iaitu keyakinan individu terhadap kesihatan awam dan vaksin, dan pengurangan imuniti dalam individu. Memandangkan faktor-faktor ini dimodelkan secara berasingan dalam kebanyakan model penyakit berjangkit, penyelidikan ini bertujuan untuk menyatukan kedua-dua keyakinan individu terhadap kesihatan awam dan vaksin, dan pengurangan imuniti dalam individu ke dalam satu model epidemiologi bagi mengekalkan imuniti kelompok. Model dalam penyelidikan ini dikenali sebagai model Susceptible-Infected-Recovered-Trust-Vaccinated-Waned (SIRTVW). Perumusan model SIRTVW menjadi Equation-Based Model (EBM) dengan Ordinary Differential Equation (ODE) bukan linear dan Individual-Based Model (IBM) dengan peraturan yang diberikan kepada individu telah dilaksanakan masing-masing dengan menggunakan MATLAB (fungsi penyelesaian ODE: ode15s) dan NetLogo. Di samping itu, penyatuan dinamik tiruan berdasarkan teori permainan ke dalam EBM dan IBM membantu keputusan vaksinasi individu. Penentusahan dan pengesahan EBM dan IBM mengaplikasi analisis sensitiviti parameter dan petunjuk prestasi seperti metrik pengukuran peratusan ketepatan Root Mean Square Percentage Error (RMSPE) dan masa pelaksanaan. Berdasarkan simulasi EBM dan

IBM dengan menggunakan parameter sebenar penyakit berjangkit Pertussis di Malaysia, sekitar 70% individu di EBM dan 80% individu di IBM mesti memperoleh keyakinan terhadap kesihatan awam dan vaksin untuk menghasilkan keputusan simulasi yang optimum apabila disahkan dengan penyebaran sebenar. RMSPE sebanyak 22.31% di IBM lebih rendah daripada RMSPE sebanyak 56.12% di EBM disebabkan oleh heterogenitas individu dalam IBM yang mana EBM tidak mengambil kira. Memandangkan IBM meniru penyebaran sebenar, simulasi IBM yang 36.36% lebih perlahan daripada EBM boleh diterima. Tambahan pula, keyakinan individu terhadap kesihatan awam dan vaksin, dan kecenderungan individu untuk melindungi diri daripada jangkitan boleh mengurangkan penularan penyakit berjangkit dalam populasi. Berkaitan dengan imuniti kelompok, satu formula ambang imuniti kelompok yang diubah suai telah diperoleh daripada model SIRTVW. Pengubahsuaian terhadap formula imuniti kelompok menghasilkan nilai ambang yang berbeza disebabkan oleh kepekaan parameter tertentu yang termasuk dalam formula. Memandangkan ambang imuniti kelompok digunakan untuk menentukan bilangan minimum individu yang sepatutnya imun untuk mendorong imuniti kelompok, ambang imuniti kelompok daripada formula yang diubah suai memberikan pandangan baharu untuk penubuhan imuniti kelompok. Adalah sangat penting untuk mengekalkan penubuhan imuniti kelompok dalam populasi kerana kehilangan imuniti kelompok menjadi penghalang dalam mengawal penularan penyakit berjangkit.

Kata kunci: *Imuniti kelompok, ambang imuniti kelompok, keyakinan individu, pengurangan imuniti, pemodelan penyakit berjangkit*

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LIST OF ABBREVIATIONS

ABM	Agent-Based Model
CSV	Comma Separated Values
DFE	Disease Free Equilibrium
EBM	Equation-Based Model
GIS	Geographical Information System
IBM	Individual-Based Model
NDFs	Numerical Differentiation Formulas
ODE	Ordinary Differential Equation
OS	Operating System
PDE	Partial Differential Equation
RAM	Random Access Memory
RMSPE	Root Mean Square Percentage Error
SIR	Susceptible-Infected-Recovered
SIRTVW	Susceptible-Infected-Recovered-Trust-Vaccinated-Waned

CHAPTER 1

INTRODUCTION

1.1 Research Background

Infectious diseases are the illnesses which can be transmitted from one individual to another individuals, resulting from infections caused by pathogenic microorganisms such as viruses, bacteria, fungi and parasites (World Health Organization, 2020). The frequent outbreaks of infectious diseases have been alarming and become major public health concerns around the world. Even though most of the infectious diseases are controllable by vaccines (which is known as vaccine-preventable diseases), the unexpected outbreaks still cause morbidity and mortality in the population. People who have greater risk to become infected such as newborns, infants and elders are more vulnerable towards infectious diseases and might develop serious complications after infection.

The main control measure introduced to overcome the infectious diseases outbreaks is done through vaccination program. It is a must to ensure that all individuals in the population receive the recommended vaccination at the right age and time (Centers for Disease Control and Prevention, 2016). Despite the introduction of vaccination program for infectious diseases, it remains as the global challenge for the public health to control the outbreaks. People continue to be at risk unless the infectious diseases are eradicated. Public health sometimes is not confident whether the proper vaccination coverage is achievable as they have difficulties in monitoring the vaccination coverage. Recognizing that 100% vaccination coverage is never reachable, the main concern of public health is to achieve the real herd immunity establishment in the population (Gostin, 2019).

Herd immunity comprises of two words namely ‘herd’ (a group or community) and ‘immunity’ (individual’s resistance against infection of pathogenic microorganisms). In the context of infectious diseases epidemiology, the herd immunity is the resistance from getting infected by infectious diseases due to the presence of high number of immune individuals, thus reducing the probability of infected individuals encounter with susceptible individuals (Anderson, 1992; Fine et al., 2011; Balakrishnan & Rekha, 2018; Vyas et al., 2020). The herd immunity can be categorized into two different types namely innate herd immunity and acquired herd immunity, based on the source of immunity obtained by the immune individuals. The immune individuals with immunity determined by genetic inheritance or physiological changes of the individuals establish the innate herd immunity, while the acquired herd immunity is formed when the immune individuals develop immunity through vaccination or natural infection (Balakrishnan & Rekha, 2018).

Generally, the term ‘herd immunity’ mostly refers to the acquired herd immunity. The immune individuals are the individuals with immunity against infectious diseases, who have either vaccine-induced immunity (by means of vaccination) or infection-induced immunity (by means of natural infection). The presence of enough immune individuals in the population induces herd immunity which acts as a barrier in controlling the transmission of infectious diseases and therefore indirectly protects the susceptible individuals from infection. For instance, the herd immunity gives protection to newborns, infants, elders and those people with severe diseases who cannot take vaccination to be immune. Although these people are not immune, they are still protected from infectious diseases through the herd immunity establishment. The visualization on how herd immunity works in the population can be seen in Figure 1.1.

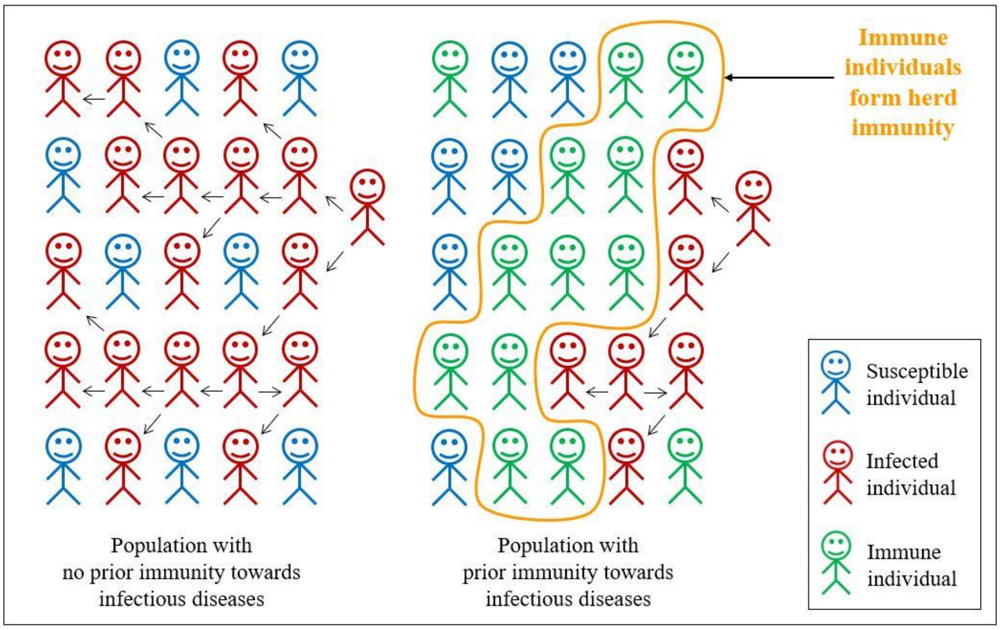

Figure 1.1: The visualization of herd immunity

Due to this fact, the concept of herd immunity is widely used in designing vaccination program to eliminate infectious diseases. Even though both vaccination and natural infection contribute to the number of immune individuals in the population, it is more rational to target and increase the number of immune individuals via vaccination rather than infection. This is because the number of immune individuals resulting from infection is unpredictable and based on the transmission of infectious diseases. In order to overcome the spread of infection, the minimum number of immune individuals required to induce herd immunity depends on the herd immunity threshold I_c that defines the critical proportion of immune individuals needed to eradicate the infection (Anderson, 1992; Fine et al., 2011; Balakrishnan & Rekha, 2018; Fine et al., 2018; Masterson et al., 2018; Vyas et al., 2020). Hence, it is not compulsory to vaccinate everyone in the population to become immune. However, it is necessary to ensure that the number of immune individuals in the population is enough for establishing herd immunity so that the others who are not immune can also be protected against infectious diseases.

Unfortunately, there are few factors happened in these recent years that affect herd immunity establishment and result in the re-emergence of infectious diseases in the population. The first factor that has influence on the herd immunity is the individual behaviour of vaccine-refusal group in vaccination decision. Despite availability of vaccines, the growth of vaccine-refusal group or delaying vaccines in the society gives a negative impact in maintaining herd immunity (Nabet et al., 2017). The reasons of refusing vaccination are mainly due to several factors such as low trust in public health and vaccines (Damnjanovic et al., 2018), vaccine safety concerns (Abu-Rish et al., 2016; Damnjanovic et al., 2018), past experiences with vaccination (Boes et al. 2017), barrier to vaccination (Mohd Azizi et al., 2017) and free-riding (Pietro et al., 2017). The lack of trust in public health and vaccines causes a major health emergency in Democratic Republic of the Congo during the Ebola virus outbreak (The Lancet Infectious Diseases, 2019). As for the free-riding problem, some parents feel that their children do not need to take vaccine if the other children are vaccinated, assuming their children would benefit from herd immunity (Pietro et al., 2017). The individual behaviour of hesitancy or refusal in vaccination leads to a smaller number of individuals getting vaccinated. As a result, the number of immune individuals becomes lower while the number of susceptible individuals keeps increasing. Thus, the herd immunity might disappear from the population and causes the outbreaks of infectious diseases.

Another problem which impacts the herd immunity establishment is the wane of immunity in individuals referring to the waning of vaccine-induced immunity and infection-induced immunity from the body. The waning of vaccine-induced immunity is one of the factors for the re-emergence of childhood infectious diseases (Hamami et al., 2017; Lewnard & Grad, 2018). The duration of immunity provided by vaccine varies according to different type of infectious diseases and its vaccines. The suggested timing of vaccine doses focuses to provide the best protection when the exposure to the infection is the highest. However, for some infectious diseases such as Pertussis and Diphtheria, both vaccine-induced and infection-induced immunities do not guarantee a life-long protection against infection. When the immunity wanes, it increases the number of susceptible individuals in the population. As a result, the presence of immune individuals is not enough to establish herd immunity and increases the possibility for infectious diseases outbreaks in the population.

In summary, there are two factors that influence the herd immunity establishment in the population namely individual behaviour of vaccine-refusal group in vaccination decision and wane of immunity in individuals. Therefore, these factors are considered in the research to develop an epidemiological model to maintain herd immunity.

1.2 Research Problem

Behaviour of individuals against vaccination plays a big role to determine the success of vaccination program and induce herd immunity in the population. The research considers one of the individual behaviour of vaccine-refusal group in vaccination decision which is lack of trust in public health and vaccines into infectious disease modelling. The individuals' trust in public health and vaccines influences the individuals to vaccinate and take health control measures against infection. Moreover, the wane of immunity in individuals becomes one of the reasons for infectious diseases outbreaks due to high number of susceptible individuals in the population has caused herd immunity to disappear. From computational science view, there is no consolidation among modelling of individuals' trust in public health and vaccines with modelling of wane of immunity in individuals focusing on herd immunity. Thus, there is a need to integrate both factors into one epidemiological model with the aim to maintain the establishment of herd immunity.

The consideration of individual behaviour into infectious disease modelling indicates that the population is heterogenous where the individuals in the population behave in different ways. However, the basic Susceptible-Infected-Recovered (SIR) model, which is an Equation-Based Model (EBM), used in most infectious disease modelling has limitation to capture the heterogeneous characteristics due to the assumption that the population is homogeneous and well-mixed (Trawicki, 2017). Hence, an Individual-Based Model (IBM) can also be used in infectious disease modelling to capture heterogeneity in the population.

1.3 Research Objective

Several objectives have been designed to solve the research problem. The objectives of the research are given as follows:

i. To formulate an epidemiological model consolidating individuals' trust in public health and vaccines as well as wane of immunity in individuals.

ii. To govern the model formulation in (i) into EBM of non-linear Ordinary Differential Equation (ODE) and IBM of rules assigned to the individuals.

iii. To derive a modified formula of herd immunity threshold I_c from (i) and (ii).

iv. To implement (i), (ii) and (iii) through MATLAB (ode15s) and NetLogo.

v. To perform verification and validation for EBM and IBM of the model by using parameter sensitivity analysis and performance indicators.

vi. To determine the value of the modified herd immunity threshold I_c formula by using parameter sensitivity analysis.

1.4 Research Hypothesis

In order to address the research problem based on the research objectives, it is claimed that there is a possibility to consolidate the modelling of individuals' trust in public health and vaccines with the inclusion of wane of immunity in individuals into one epidemiological model focusing on the maintaining of herd immunity. As mentioned before, the individuals' trust in public health and vaccines affects the vaccination decision of individuals. Therefore, the formulation of the model involves the modification of the basic SIR model to incorporate individuals' trust in public health and vaccines, vaccination decision due to trust behaviour and wane of immunity in individuals altogether into a model. The model formulation which has been governed into EBM of non-linear ODE and IBM of rules assigned to the individuals is hypothesized to have impact on the transmission of infectious disease. The simulation results for EBM and IBM of the model via MATLAB and NetLogo respectively might be varied throughout verification and validation by using parameter sensitivity analysis and performance indicators due to the effects of individuals' trust, vaccination decision and wane of immunity. Moreover, the interactions between individuals in IBM corresponding to the assigned rules and heterogeneity of individuals are believed to generate simulation results that mimic the actual prevalence of infectious disease. Besides that, the modified formula of herd immunity threshold I_c for determining the critical proportion of immune individuals required to induce herd immunity can be derived from the model. The parameter sensitivity analysis carried out to the modified herd immunity threshold I_c formula is hypothesized to generate different values and provides new insights on the determination of immunity values corresponding to the population for establishing herd immunity. In conclusion, the consolidation of individuals' trust in public health and vaccines as well as wane of immunity in individuals into one epidemiological model